The ELiPSE-1 Study: A Phase 1, Multicenter, Open-label Study of CNTY-101 in Subjects with Relapsed or Refractory CD19-positive B-cell Malignancies (#407030)

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Clinical Trial information: NCT05336409. 1. Swedish Cancer Institute Seattle, WA; 2. Century Therapeutics Philadelphia, PA; 3. MD Anderson Cancer Center Houston, TX; 4. Henry Ford Health Detroit, MI

Background:
Century Therapeutics’ (Century) foundational induced pluripotent stem cells (iPSCs) platform enables multistep clustered regularly interspaced short palindromic repeats (CRISPR)-nuclease driven homology directed repair cellular engineering to produce a highly homogeneous master cell bank (MCB) of modified cells with virtually unlimited self-renewing capacity. The MCB can be expanded and differentiated into desired immune effector cells, sufficient for the lifetime of the homogeneous allogeneic therapeutic product. This platform is differentiated from allogeneic approaches that utilize non-renewable donor-derived cells, where gene editing must be repeated for each batch.

Multi-step editing enables optimization of
- cell performance,
- persistence, and
- target recognition.

Through this innovative platform, Century aspires to address limitations of current therapies.

CNTY-101 is an allogeneic cellular immunotherapy product consisting of ex-vivo genetically-engineered NK cells expressing as transgenes: an anti-CD19 CAR, human leukocyte antigen (HLA) E, secretable interleukin 15 (IL-15), and a short epidermal growth factor receptor (sEGFR) variant containing the cetuximab binding epitope as the safety switch. Expression of HLA Class I and II has been disrupted through genome editing at beta-2 microglobulin (β2M) and the Class II transactivator (CIITA), respectively.

Methods:
This first-in-human study will determine the maximum tolerated dose (MTD) and recommended Phase 2 regimen (RP2R) of CNTY-101 in combination with subcutaneous (SC) IL-2 in patients with R/R aggressive and indolent CD19-positive B-cell Non-Hodgkin lymphomas who are without other treatment options, including patients with
- diffuse large B-cell lymphoma (de novo and transformed from indolent NHL),
- mantle cell lymphoma,
- primary mediastinal large B-cell lymphoma,
- follicular lymphoma, and
- marginal zone lymphoma.

In addition to safety and efficacy endpoints, the trial will evaluate translational endpoints including the following:
- CNTY-101 cellular kinetics in Schedule A vs Schedule B, following single vs multiple cycles
- Enumeration of B cells pre- and post-infusion.
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  - CNTY-101 cellular kinetics in Schedule A vs Schedule B, following single vs multiple cycles
  - Enumeration of B cells pre- and post-infusion.
  - CNTY-101 iNK trafficking to the tumor and changes in the tumor microenvironment associated with response or resistance
  - Preexisting and emerging humoral and cellular immune responses to CNTY-101
  - Serum cytokines previously shown to be associated with CRS and ICANS, or cell expansion and response